Appl. No. 10/588,220 Atny. Ref.: 1487-29

Amendment After Final Rejection

February 7, 2010

AMENDMENTS TO THE CLAIMS:

Please amend the claims as follows:

Claims 1-113. (Cancelled)

114. (Currently Amended) A process for screening glycoform specific antibodies capable of binding to at least one given glycoform of a second glycoprotein among antibodies elicited against a first glycoprotein.

said first glycoprotein being pituitary or blood human TSH from healthy individuals.

said second glycoprotein being a recombinant human TSH produced by mammalian cells and said second glycoprotein being itself a glycoform of the first glycoprotein,

said process comprising the following steps a step of determination of the binding between:

a) checking that a panel of antibodies elicited against the first glycoprotein bind to said recombinant human TSH, said antibodies being classified in pools, each pool being characterized in that two antibodies selected from the same pool can not bind to the same glycoprotein at the same time.

(1) contacting said panel of antibodies elicited against the first glycoprotein with at least one glycoform of said recombinant human TSH.

(2) determining the binding affinity between the first glycoprotein and said recombinant human TSH, or at least one glycoform of said recombinant human TSH, and

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recovering antibodies recognizing said recombinant human TSH, or at least one glycoform of said recombinant human TSH with a higher affinity than that displayed with the first glycoproteinb)—at least one glycoform of a second glycoprotein.

wherein said at least one glycoform of said recombinant human TSH is the second glycoprotein is selected from a group of glycoforms of said recombinant human TSH the second glycoprotein, each glycoform of said group corresponding to a determined glycosylation state beingwhich is either:

- a) essentially more sialylated, more branched and less fucosylated than the recombinant human TSH said-second glycoprotein, or
- b) essentially more sialylated, less branched and less fucosylated than the recombinant human TSHsaid-second alveopretein.

wherein antibodies elicited against the first glycoprotein which bind to the second glycoprotein with an affinity higher than the binding affinity of said antibodies to the first glycoprotein are screened.

- 115. (Currently Amended) The process according to claim 114, wherein a glycoform of <u>said recombinant human TSH is</u> the second glycoprotein being:
- a) essentially more sialylated, more branched and less fucosylated than the recombinant human TSHsaid-second-glycoprotein, or
- b) essentially more sialylated, less branched and less fucosylated than <u>the</u> recombinant human TSHsaid second glycoprotein, and

is obtained by a combination

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of at least one enzymatic modification of <u>recombinant human TSH</u>the second elycoprotein, and/or

of at least one lectin fractionation of the second glycoprotein.

116. (Previously Presented) The process according to claim 115, wherein the lectin is selected from the group consisting of a mannose-specific lectin, a fucose-specific lectin, a gactose-specific lectin, and a sialic acid-specific lectin.

117. (Previously Presented) The process according to claim 115, wherein the enzymatic modification is carried out by an enzyme selected from the group consisting of

a glycosidase, and

a glycosyltransferase.

118. (Previously Presented) The process according to claim 117, wherein the glycosidase is a neuraminidase or a fucosidase, and wherein the glycosyltransferase is a sialyltransferase.

119. (Currently Amended) The process according to claim 115, wherein [[a]]said less fucosylated glycoform of recombinant TSH the second glycoprotein as compared to the second glycoprotein is obtained by lentil fractionation and of the second glycoprotein by collecting [[a]]the fraction which does not bind to lentil.

120. (Currently Amended) The process according to claim [[115]]131, wherein a ConA fractionation of said recombinant human TSH the second glycoprotein is performed by collecting three fractions, A, B, and C, the binding of which to ConA is such that.

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fraction C binds to ConA more strongly than fraction B binds to ConA, and

fraction B binds to ConA more strongly than fraction A binds to ConA,

the branching state of a given fraction being essentially different from the

more sialylated glycoform of said recombinant human TSH the second glycoprotein as

121. (Currently Amended) The process according to claim [[114]]115, wherein a

compared to the second glycoprotein is obtained by sialyltransferase treatment of said

second-glycoprotein or by neuraminidase treatment followed by sialyltransferase

treatment of said second glycoprotein.

branching state of the other two fractions.

122. (Currently Amended) The process according to claim 115 or 121, wherein

the sialyltransferase is a $\alpha\text{--}2,6\text{--sialyltransferase}$ having an increased solubility and a

superior activity.

123. (Currently Amended) The process according to claim 122, wherein said α -

2,6-sialyltransferase is a N-terminally shortened ST6Gall sialyltransferase having

deleted of at most its first 99 residues as set forth in SEQ ID NO: 1.

Claim 124. (Canceled)

Claim 125. (Canceled)

126. (Currently Amended) The process according to claim 114, wherein the

binding of the antibodies to the first glycoprotein, to the recombinant TSH and to the

glycoforms of the recombinant TSH antibody binding is determined by immunoassays.

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127. (Currently Amended) The process according to claim 126, wherein the

immunoassays are immunoassay formats comprising comprise an amplification system

for detection.

128. (Currently Amended) The process according to claim 126 or 127, wherein

the immunoassays are [[is a]] sandwich immunoassays, comprising the following steps:

fixing a capture antibody selected from a pool onto a solid phase obtained in a

preliminary step, said preliminary step being such that the antibodies to be screened are

elassified in pools, each pool being characterized in that two antibodies selected from

[[a]]the same pool can not bind to the same glycoprotein at the same time,

onto a support,

contacting a glycoprotein, corresponding to the first glycoprotein, to the

recombinant TSH second glycoprotein or to the glycoforms of the recombinant

TSH second glycoprotein, to said capture antibody, to form a capture antibody-

glycoprotein binary complex,

contacting a tracer antibody, selected from a pool obtained in a preliminary step.

said preliminary step being such that the antibodies to be screened are classified in

 $\underline{\text{pools}},$ each pool being characterized in that two antibodies selected from [[a]] $\underline{\text{the}}$ same

pool can not bind to the same glycoprotein at the same time, provided said pool is

different from the one used for the selection of said capture antibody, to said capture

 $antibody-glycoprotein\ binary\ complex,\ to\ form\ a\ capture\ antibody-glycoprotein-tracer$

antibody ternary complex,

detecting the tracer antibody for measuring the number of temary complexes.

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129. (Previously Presented) The process according to claim 116, wherein the lectin is selected from the group consisting of a ConA lectin, a Lentil lectin, an Ulex lectin, a ricin, a limulin lectin and a Sambucus nigra lectin.

- 130. (Previously Presented) The process according to claim 127, wherein the immunoassays are an ELISA format.
- 131. (new) The process according to claim 116, wherein the manose-specific lectin is ConA.